REMARKS

Applicants' Attorney notes with appreciation the telephonic interview granted by the Examiner and conducted on December 16, 2008. Accordingly, claim 1 has been amended to recite a food and feed supplement comprising, *inter alia*, "at least one C_{1-8} carboxylic acid and/or its salt . . . the B_6, B_9 and B_{19} vitamins . . . wherein the combined amounts of the vitamins B_6, B_9 and B_{12} are respectively in the range of 0.5-30 mg, 0.1-10 mg and 1-1500 μg/gram dry weight of the at least one C_{1-8} carboxylic acid . . . ." Therefore, requisite clarity is believed to have been provided to the correlation between the amount of the carboxylic acid and the amount of the vitamins B_6, B_9 and B_{12}. Potential uncertainties associated with the recitation of "the COOH-groups" in claim 1 of a previous version, wherein an amount of the COOH-groups may be deemed to depend on a particular temperature or pH of a solution in which the carboxylic acids are dissolved, are therefore alleviated according to claim 1 in current form, wherein the amounts of the B vitamins respectively are recited in substantially definitive weight ratios relative to the carboxylic acids used in the supplement.

Applicants note with appreciation the withdrawal of the objections to claims 1-5 due to various informalities and the withdrawal of rejections to claims 6-8 under 35 U.S.C. § 101 because of recitation of a use without setting forth any steps involved. Applicants further note with appreciation the acknowledgment and consideration of the references submitted via Supplemental Information Disclosure Statement By Applicant dated June 16, 2008, namely DE 2559570 to Hofmann, DE 2559569 to Hofmann, Bianco et al. 1970 and Wolter 1993, English translations thereto have been recently obtained and are submitted herein as a courtesy.

Rejections under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement have been maintained to claims 1-5 and have been newly added to claims 6-8, 11-14. Rejections under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, have been maintained to claims 1-5 and have been newly added to claims 6-8, 11-14. Rejections under 35 U.S.C. §

102(b) as being anticipated by Bailey et al. (U.S. Pub. No. 2202/0150653; hereinafter *Bailey*) have been maintained to claims 1-5 and have been newly added to claims 6-8, 11-14.

By this paper, claims 2 and 11 have been newly cancelled in light of the amendment to claim 1. As such, claims 1, 3-8 and 12-14 are currently pending in the application.

Remarks Directed To Rejections To Claims 1, 3-8 And 12-14 Under 35 U.S.C. § 112, First And Second Paragraphs, With Particular Respect to the Term "C_{1-8} carboxylic acid"

The reasonings provided to the rejections as stated on pages 3-5 of the final Office Action dated October 1, 2008 are substantially similar, if not word-for-word identical, to the corresponding reasonings stated on pages 3-6 of the non-final Office Action dated December 17, 2007.

To brief, the term "C_{1-8} carboxylic acid" recited in the claims is deemed "not adequately described to convey what comprises the term" and more particularly, it is deemed unclear whether "the structure is straight . . . branched . . . a single ring . . . more than one ring . . . ." (the final Office Action, pages 3-4; the non-final Office Action, pages 3-4). The term "dry" or "dry weight of the supplement" is deemed unclear because "the specification does not provide a standard for ascertaining the requisite degree" (the final Office Action, pages 4-5; the non-final Office Action, page 5).

In response to the non-final rejections, Applicants submitted remarks in the last-filed amendment dated June 10, 2008 in an effort to illustrate support for the term "C_{1-8} carboxylic acid". Relevant portions of the remarks are reproduced below:

> By convention, C_{1-8} carboxylic acid refers to carboxylic acid having 1-8 carbon atoms. As such, the C_{1-8} carboxylic acid structurally may not contain more than one ring, regardless if it is a 5-carbon ring or a 6-carbon ring. One example of a ring-containing C_{1-8} carboxylic acid is a benzoic acid as indicated in paragraph [0046]. Likewise, C_{1-8} carboxylic acid is reasonably ascertained to have a straight chain structure as indicated in the

> specification in view of the list including the formic acid, the citric acid, the lactic acid, the propionic acid, the ascorbic acid, the furmaric acid. *Id.* As defined in the specification originally filed and particularly in paragraph [0046], the term C_{1-8} carboxylic acid of claim 1 may be reasonably ascertained as either straight-chained or of a ring structure. As such, requisite clarity is believed to have been provided to the term C_{1-8} carboxylic acid as recited in claim 1.
>
> (Page 5 of the Amendment dated June 10, 2008).

It is the Examiner's considered opinion that Applicants' last filed amendment dated June 10, 2008 is not persuasive and therefore the rejections to claims 1-5 under 35 U.S.C. § 112, first paragraph, are maintained. (*See* page 6 of the final Office Action.) However, what is provided as the reasons for the Examiner's opinion is nothing but a two-line sentence that is rather conclusory if not arbitrary at least to some extent: "Applicant arguments are not commensurate in scope with the claims. The art meets the composition recitations of the claims." *Id.*

> MPEP 707.07(F) in relevant portion provides:
>
> If it is ***the examiner***'s considered opinion that the asserted advantages are not sufficient to overcome the rejection(s) of record, he or she ***should state the reasons for his or her position in the record***, preferably in the action following the assertion or argument relative to such advantages. By so doing the applicant will know that the asserted advantages have actually been considered by the examiner and, if appeal is taken, the Board of Patent Appeals and Interferences will also be advised.
>
> (emphasis added).

Contrary to the guidelines provided by the relevant portions of MPEP 707.07(F) as cited above, it is not clear to Applicants as to what the purported reasonings as quoted above really amount to or why the Applicants' relevant remarks are not considered persuasive.

However, in order to move the prosecution forward, claim 1 has further been amended to read, *inter alia*, "wherein the at least one C_{1-8} carboxylic acid is a formic acid, a citric acid, a lactic acid, a propionic acid, an ascorbic acid, a fumaric acid, an acetic acid, or a benzoic acid ..."

The independent claim 1 in current form recites a food and feed supplement including, *inter alia*, at least one C_{1-8} carboxylic acid being a formic acid, a citric acid, a lactic acid, a propionic acid, an ascorbic acid, a fumaric acid, an acetic acid or a benzoic acid; the B_6, B_9 and B_{12} vitamins in a combined amount of 10-50 mg/gram dry weight of the supplement, wherein the amounts of the vitamins B_6, B_9 and B_{12} are respectively in a range of 0.5-30 mg, 0.1-10 mg and 1-1500 mg per gram dry weight of the at least one carboxylic acid; 5-25 mg Fe per gram dry weight of the supplement; and 0-1 mg of an antioxidant per 100 mg dry weight of the supplement.

The above amendment is well supported in [0046] of the published application, where it states "the most useful carboxylic acid were found to be C_{1-8} carboxylic acids and the most preferred *acids* would be formic-, citric-, lactic-, propionic-, ascorbic-, fumaric- and benzoic *acid*." (Emphasis added.) The hyphens used in the above quoted portion of [0046] are clearly referred to the preferred "acids" introduced immediately before the hyphens and indicate various acids similar to benzoic acid within the family of C_{1-8} carboxylic acids.

Moreover, the term "formic-", like the other similarly positioned terms with the hyphens, clearly refers to formic acid, as [0039] of the published application illustratively shows the use of formic acid as an ingredient of the supplement according to one or more embodiments of the present invention.

In light of the instant claim amendments and the remarks stated herein, requisite clarity with regards to the term "C_{1-8} carboxylic acid" is believed to have been provided. Reconsideration and withdrawal of the rejections to claims 1, 3-8, and 12-14 under 35 U.S.C. 112, first and second paragraphs, with respect to the term "C_{1-8} carboxylic acid", is respectfully solicited.

Remarks Directed To Rejections To Claims 1, 3-8 and 12-14 Under 35 U.S.C. § 112, Second Paragraph, With Particular Respect to the Terms "Dry" and "Dry weight"

The reasonings provided to the rejections as stated on pages 4-5 of the final Office Action dated October 1, 2008 are again substantially similar, if not word-for-word identical, to the corresponding reasonings stated on pages 5-6 of the non-final Office Action dated December 17, 2007.

To brief, the term "dry" is deemed to be a "relative term which renders the claim indefinite" (the final Office Action, page 4; the non-final Office Action, page 5); the term "dry weight" is deemed unclear and "does not allow one of skill in the art to ascertain the metes and bounds of the invention" (the final Office Action, page 5; the non-final Office Action, page 5).

In response to the non-final rejections, Applicants submitted remarks in the last filed amendment dated June 10, 2008 in an effort to illustrate support for the concept of "dry weight" as used in the claims. Relevant portions of the remarks are reproduced below:

> Contrary to the contention of the Patent Office, the term "dry" or "dry weight" as recited in the claims 1-5 is commonly known and widely used to mean "the mass of a material or an object when dried and without fluids." For example, the term "dry weight" is employed in the statutory language of California Code of Regulations Section 1408.3, a copy of which has been submitted with the last amendment dated 6 May 2008. Moreover, Applicants have conducted a search, in the United States Patent and Trademark Office patent database, using the search formula of "ACLM/"dry weight" AND ACLM/"vitamin" AND ISD/20000101->20050101. The search resulted in 17 issued patents. All the 17 patents issued by the Office recite "dry weight" as a stand-alone term in the claims section without further elaborating "what is dry weight" or "how dry is dry" in respective specification of each of the issued patents. A copy of the search result has been submitted with the last amendment dated 6 May 2008. As such, Applicants submit that one skilled in the art would readily be able to ascertain that "dry weight" means the weight of a mass or an object when dried or without fluids and therefore, claims 1-5 submitted to be definite for their mere recitation of the term "dry weight."

(Pages 5-6 of the Applicants' last filed amendment dated December 10, 2008).

However, it is the Examiner's considered opinion that Applicants' last filed amendment dated June 10, 2008 is not persuasive and therefore the rejections to claims 1-5 under 35 U.S.C. § 112, first paragraph, are maintained. As stated on page 7 of the final Office Action:

> Applicant's arguments filed 6/10/2008 have been fully considered but they are not persuasive. ***Applicant arguments are to other applications which do not address how the term is view[ed] in the instant application.*** Additionally, the specification recites pH ranges when used in water which is not dry, and the claims are open language which allows for carriers and solvents which goes to the indefinite of "dry weight" and "dry weight of the composition" and it is not clear what forms (e.g. powder verses solution) or components the composition is restricted to.
>
> (emphasis added).

What was submitted to the Patent Office, along with the remarks quoted above, was to provide support that the term "dry weight" or "the dry weight of the composition" is well known in the art.

As shown in co-inventor Frode Brakstad's Declaration submitted herewith, "the concept of "dry weight" with respect to the determination and the application thereto is well known in the art. In fact, the meaning of "dry weight" and the calculation thereof can be easily found in encyclopedias and on the internet" (paragraph 5 of the Declaration).

As further shown in the Declaration, the term "dry weight", as used in biology, fool science, and other fields, refers to the dry matter mass of a composition when completely dried. For example, the dry matter of a piece of bread is its solids, i.e. all its constituents excluding water. The dry matter constituents of the bread may include proteins, fats, sugars, and minerals" (paragraph 6 of the Declaration).

As further shown in the Declaration, "a plant, animal, or other composition containing a chemical constituent of interest is dried to remove all water from the composition. The amount of the chemical constituent found in subsequent analysis is then expressed as weight of the chemical constituent divided by weight of the dried composition which once contained the chemical constituent" (paragraph 7 of the Declaration).

As further shown in the Declaration, "to remove all the water, various methods can be used. For example, a composition may be heated upon a certain temperature, such as above 100 degrees Celsius, to evaporate the water molecules out of the composition. Similarly, a composition may also be subject to a desiccating compartment to dry out the water molecules over time or be subject to a drying oven with medium to high heat if the composition is relatively heat resistant. Requisite completeness of the drying is ascertained when weight of the composition due to solvent removal such as water removal no longer changes" (paragraph 8 of the Declaration).

As further shown in the Declaration, "calculations involving dry weight of a composition are routinely carried out in various research laboratories, nutrition clinics, and animal study facilities that I know of and or am affiliated with" (paragraph 9 of the Declaration).

Based on the remarks stated herein, Applicants respectfully submit that the extent of dryness and the determination of dry weight, in practicing one or more embodiments of the present invention, can be readily ascertained based on the known knowledge in the art as stated above.

Moreover, MPEP 2164.01 in relevant portion provides:

> ***A patent need not teach and preferably omits, what is well known in the art.*** *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

(emphasis added).

Therefore, the term "dry weight" recited in the present claims are well known in the art according to the submissions previously made and as identified above. Consequently, the present specification needs not include and should indeed preferably omit, within the language of MPEP 2164.01 cited above, descriptions as to what constitutes "dry weight" or how "dry weight" should be determined. To say "Applicant arguments are to other applications which do not address how the term is view[ed] in the instant application" is, therefore, misplaced.

It is also misplaced to state that the claims fail to specify what forms (e.g. powder verses solution "the composition is restricted to." *Id.* A claim only needs to recite elements essential for what the Applicants regard as the invention. Clearly, claim 1, being a composition claim, recites a supplement comprising the listed essential elements. However, there is no need to restrict the supplement as powder or solution, simply because both may be used and functional. The instant specification has provided ample examples as to what the supplement may be in and how the supplement may be used. The food and feed supplement according to one or more embodiments of the present invention, may be used in several different forms as illustrated below.

As shown in [0028] - [0029] of the published application 2007/0166355, racing pigeons show much improved performance scores once they are fed with a supplement including carboxylic acids, B_6, B_9, B_{12} vitamins, and iron Fe. As demonstrated in [0031], previously sick horses show improvement in gastric/intestinal mucosa lesions upon the administration of the supplement added in an amount of 5-25 grams per 100 kg horse weight. As demonstrated in [0033], racing dogs show reduced signs of anemia and improved levels of blood cells upon the administration of the supplement in an amount of 1.0-1.5 grams per dog. As demonstrated in [0034] - [0037] of the published application, examples of recommended B vitamin and iron content in the supplement according to one or more embodiments of the present invention are provided with respect to poultry, pigeons, pigs, cattle, sheep, fish, horses and rabbits. As demonstrated in [0038] - [0040] of the published application, patients previously diagnosed with rheumatism report much reduced pain and increased vitality, upon the administration of formic

acid containing supplement with daily intake of 3mg per kg body weight. As demonstrated in [0041] to [0044] of the published application, examples of suitable dosing for B_6, B_9, B_{12}, and Fe are provided with regards to variable species including pigeon, human, horse and dog.

Additionally, the recitation of "the amount of the carboxylic acid and/or its salt will give a pH of 2.0 - 6.0 when the supplement is dissolved in water," does not by itself necessitize either expressly or impliedly, the need for the supplement to be in a liquid form. Rather, this recitation concerns that the amount of the carboxylic acid, and along with B vitamin having amounts corresponding thereto, is determined such that a particular pH range of 2.0 - 6.0 results when all the ingredients of the supplement are dissolved in water, such as when the supplement is taken by a subject and dissolved in the gastrointestinal system of the subject.

Therefore, the supplement according to one or more embodiments of the present invention has been described with ample details as to how it may be prepared and used.

In light of the above remarks and the instant claim amendments, reconsideration and withdrawal of the rejections to claims 1, 3-8, and 12-14, under 35 U.S.C. 112, second paragraph, with particular respect to the terms "dry" or "dry weight", is respectfully solicited.

Remarks Directed to Rejections to claims 1, 3-8, and 12-14 under 35 U.S.C. 102(b) over Bailey

Bailey concerns compositions for supplying folate having a natural isomer of reduced folate which includes variable tetrahydrofolic acids and their polyglutamyl derivatives (Abstract; [0008]). Natural isomer means a tetrahydrofolate having the natural configuration at both the glutamate α- and the pteridine 6-carbons ([0033]).

According to *Bailey*, "the form of folate currently added to all commercial vitamin preparations or which is added to foods, folic acid (I) . . . is not one of the major forms found in natural fresh foods. The structure of folic acid (I) differs from the most abundant natural folate in several aspects" ([0006] - [0007]); "when folic acid (1) is absorbed by the digestive tract it is

eventually reduced to active (6S) - tetrahydrofolic acid (II) by the enzyme dihydrofolate reductase" ([0009]); "chemical reduction of folic acid (I) produces a nearly racemic mixture of the two isomers at this position . . . Compounds II - VIII are shown as the natural isomer . . . The effect of a long term exposure to the unnatural isomer of reduced folate is unknown" ([0012]); "an object of this invention is nutritional compositions in which the natural isomer of tetrahydrofolic acid, or a derivative thereof, is substituted for the usual folic acid (I) . . . the average health of the population, will be improved by addressing the needs of those for whom folic acid (I) bioavailability is poor" ([0016]).

These *Bailey* compositions can be presented in combination with a nutritional substance including a food preparation or an essential nutrient preparation ([0020]). According to *Bailey*, "essential nutrient preparation are materials which contain one or more essential nutrients . . . essential nutrients are those nutrients which are required to sustain health but which cannot be effectively produced by one or more animals or by humans . . . suitable essential nutrient preparations are ... typically available commercially in the form of pills, tablets, capsules, powders, syrups, and suspensions ([0020]); and "food preparations are materials which contain one or more amino acid, carbohydrate, or fat, which are suitable for human or animal consumption, and which are not essential nutrient preparations" ([0021]).

Various examples of *Bailey* compositions are given to illustrate how the concept of natural isomer of reduced folates (or tetrahydrofolates) can be put into use. Example 1 relates to a ready to eat breakfast cereal containing, among other things, 0.114 mg of 5-methyl-6(s) tetrahydrofolic acid (III) disodium salt per a 30g serving ([0040]). Example 2 relates to a multivitamin tablet containing, among other things, 0.437 mg of 5-methyl-6(s)-tetrahydrofolic acid (III) magnesium salt per tablet ([0041]). Example 3 relates to a multivitamin and minerals tablet containing, among other things, 0.545 mg 5-formyl-(6s)-tetrahydrofolic acid (IV) cacium salt-pentahydrate per tablet.

At various places, *Bailey* introduces the use of reduced iron ([0040]), vitamin B_{12} ([0041]), citric acid ([0042]), ascorbic acid ([0043]), vitamin D_3 ([0044]), and vitamin E ([0047]). However, *Bailey* does not seem to teach the use of vitamin B_6, vitamin B_9, nor does

Bailey teach the requisite arrangement of those components as recited in claim 1, let alone those components arranged and provided with the particular amounts as specified in claim 1. MPEP 2131.01 in relevant portion provides that anticipation of a claim is found only when "each and every element ***as set forth in the claim*** is found, in a single prior art reference." Please see also a recent decision delivered by the Federal Circuit on October 20, 2008, Net MoneyIN Inc. v. VeriSign Inc. The court there held that an anticipation reference must disclose all elements of claim ***within four corners of single document*** and must disclose those elements arranged as in the claim and that all limitations must be arranged or combined ***in same way as recited in claim***, not merely in particular order.

Since *Bailey* fails to teach or suggest each and every element as set forth in the independent claim 1, *Bailey* fails to anticipate claim 1 and all the claims dependent therefrom for at least the aforementioned reasons.

Reconsideration and withdrawal of the rejections to claims 1, 3-8, and 12-14 under 35 U.S.C. 102(b) over *Bailey* is solicited.

CONCLUSION

Applicants have made a genuine effort to respond to each of the Patent Office's rejections in advancing the prosecution of this case. Applicants believe that all formal and substantive requirements for patentability have been met and that this case is in condition for allowance, which action is respectfully requested. If a telephone or video conference would help expedite allowance or resolve any additional questions, such a conference is invited at the Patent Office's convenience.

The Petition fee of $65.00 is being charged to Deposit Account No. 02-3978 via electronic authorization submitted concurrently herewith. The Commissioner is hereby authorized to charge any additional fees or credit any overpayments as a result of the filing of this paper to Deposit Account No. 02-3978.

Respectfully submitted,

FRODE BRAKSTAD et al.

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ENGLISH TRANSLATION TO THE CITED REFERENCE

"DE 2559569 TO HOFMANN",

PROVIDED BY WAY OF COURTESY

[Text written vertically, 2 x: DT 25 59 569 A 1]

61 Int. Cl. [2] A23 K 1/18

19 FEDERAL REPUBLIC OF GERMANY

GERMAN PATENT OFFICE

[Stamp: almost illegible, possibly reads "Behördeneigentum" – government property]

11 PATENT APPLICATION OPEN TO PUBLIC INSPECTION 25 59 569

21 Application number: P 25 59 569.1
22 Filing date: 22.10.75
43 Publication date: 28.4.77

30 Convention priority:
32 33 31 ---

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54 Title: Liquid feed for carrier pigeons

62 Divisional application from: P 25 47 181.2

71 Applicant: Hofmann, Josef, D-8752[1] Mömbris

72 Inventor: As applicant

4.77. 709 817/642 3/70
ORIGINAL INSPECTED

1 Translator: N.B. German post codes have changed since the date of this application

Patent claim

Liquid feed for carrier pigeons, consisting of an aqueous solution of

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Liquid feed for carrier pigeons

The invention concerns a new liquid feed for carrier pigeons, containing vitamins.

Breeders are aware that the growth, production, performance and appearance of carrier pigeons are very highly dependent on the type of feed given to them. It is important in this context that the carrier pigeons are not only supplied with the basic nutrients, carbohydrates, fats, proteins, but also with vitamins, minerals and amino acids. An additional decisive factor for the achievement of the desired result is that the composition of the feed is made up in a qualitatively optimum fashion.

The most important carbohydrates are starch, mono- and disaccharides and also glucose and sucrose. Several fatty acids in fat are vitally important to the animal body. But these essential fatty acids, which the animal is not able to synthesise itself, are present in sufficient quantities in the feed. The body can form a fairly large number of the amino acids essential for the maintenance of vital functions from other amino acids. But certain amino acids have to be given in the diet since the body is not able to construct them. These include lysine, for example.

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In addition to the organic nutrients, minerals, such as sodium, potassium, calcium, magnesium and phosphorus are also essential constituents of the diet. Very small quantities of iron, copper, zinc, manganese, cobalt and iodine are also required for metabolic functions to progress normally. These are known as trace elements.

The higher the load on the body, the greater its requirement for vitamins. Since it is unable to synthesise these itself, they must also be supplied in the feed.

The invention is based on the problem of making available a feed for carrier pigeons that is adapted to a wide variety of conditions as regards the animals and to the changing requirements made of the pigeons.

This problem is resolved by the liquid feed in accordance with the patent claim.

The constituents of the feed in accordance with the invention provide strength and performance and have a favourable influence on the animal metabolism.

The feed can be made up by combining the individual constituents. But it can also be put together from previously combined mixtures or partial mixtures of desired feed constituents. For example, mixtures of the active substances can be obtained from the extract of freshly harvested sugar beets.

The feed in accordance with the invention is particularly useful for providing vitamins to the pigeons, for achieving an optimum feather structure and for rearing young pigeons, as well as for use as a strength-giving feed for short, medium and long-distance flights.

Below is an example of quantitative composition of the feed in accordance with the invention. This feed is produced using the extract of freshly harvested sugar beets,

Example:

ENGLISH TRANSLATION TO THE CITED REFERENCE

"DE 2559570 TO HOFMANN",

PROVIDED BY WAY OF COURTESY

[Text written vertically, 2 x: DT 25 59 570 A 1]

61 Int. Cl. [2] A23 K 1/18

19 FEDERAL REPUBLIC OF GERMANY

GERMAN PATENT OFFICE

[Stamp: almost illegible, possibly reads "Behördeneigentum" – government property]

11 PATENT APPLICATION OPEN TO PUBLIC INSPECTION 25 59 570

21 Application number: P 25 59 570.4
22 Filing date: 22.10.75
43 Publication date: 28.4.77

30 Convention priority:
32 33 31 ---

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54 Title: Travel preparation for pigeons

62 Divisional application from: P 25 47 181.2

71 Applicant: Hofmann, Josef, D-8752[1] Mömbris

72 Inventor: As applicant

4.77. 709 817/643 2/70

[1] Translator: N.B. German post codes have changed since the date of this application. This applies throughout the translation.

Patent claim

Travel preparation for carrier pigeons, in powder form, consisting of

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- 2 -

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Josef Hofmann, D-8752 Mömbris-Brücken, Hemsbacher Str. 17

Travel preparation for carrier pigeons

The invention concerns a travel preparation for carrier pigeons.

Breeders are aware that the growth, production, performance and appearance of carrier pigeons are very highly dependent on the type of feed given to them. It is important in this context that the carrier pigeons are not only supplied with the basic nutrients, carbohydrates, fats, proteins, but also with vitamins, minerals and amino acids. An additional decisive factor for the achievement of the desired result is that the composition of the feed is adjusted to the load and condition of the pigeon at the time. A feed that is suitable to strengthen the pigeon in its home loft during a fairly long recovery period may not be the optimum feed for a long-distance flight.

The invention is based on the problem of creating a feed for carrier pigeons that is particularly suitable as a travel preparation.

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The travel preparation for carrier pigeons in accordance with the invention is characterised in the patent claim.

It has been found that the travel preparation in accordance with the invention, which is particularly high in vitamins, prepares the pigeons optimally for their journey.

Below is an example of the quantitative composition of the travel preparation in accordance with the invention.

Example:
The dry mixture contains the following quantities per g

x in powder form, soluble in cold water

ENGLISH TRANSLATION TO THE CITED REFERENCE

"BIANCO et al. 1970",

PROVIDED BY WAY OF COURTESY

MINERVA MEDICA

Therapy

Clinical results with a new synthetic preparation in the treatment of rheumatic disease

G. BIANCO – R. MARCOLONGO – N. DI PAOLO

Istituto di Clinica Medica Generale e Terapia Medica dell'Università di Siena (Institute of General Clinical Medicine and Medical Treatment at the University of Siena)
(Director: Prof. F. Marcolongo)

In spite of the progress made over recent years, rheumatic disease continues to cause doctors and rheumatologists numerous problems of a clinical, etiopathogenetic and above all therapeutic nature. In fact, although the vast amount of experimental research, clinical results and improvements in diagnostic methods have allowed a better understanding of certain pathogenetic aspects of rheumatic disease, treatment has still not been able to fully reflect the additional information obtained about the pathogenetic aspect. Consequently the problem of treating rheumatic disease is a subject which is still wide open and causes problems of varying degrees for doctors and rheumatologists on a daily basis. It is actually well known how the choice of an anti-rheumatic drug often involves uncertainty, creating difficulties for the doctor given the numerous, varied side effects these types of medication generally cause[3]. The problem becomes even more of a concern when we consider that treatment of these patients is generally chronic treatment or at least long-term treatment. For these reasons, doctors and rheumatologists are always interested in new drugs with an antirheumatic action, hoping to identify products which can combine therapeutic efficacy with the absence of dangerous side-effects, allowing the possibility of long and harmless administration. This is really why drugs known as non-steroid anti-inflammatories, i.e., those compounds which by definition inhibit one or more of the symptoms of the inflammatory process have, over recent years, occupied a more and more important position in the field of treating rheumatic disorders. Amongst the substances which demonstrate that they possess characteristics allowing them to be included in this category, we wanted to test the antirheumatic action of a new drug, o-ethoxy-benzylhydrazone of pyruvic acid (etossidrazone®)[a]. In the course of clinical trials and pharmacological tests conducted on animals the preparation has shown that it possesses an antiphlogistic and antalgesic action clearly better than that of acetylsalicylic acid and aminopyrine. On the other hand its antipyretic action was negligible. It also showed that it did not exercise any damaging action on the most important tissues or on the most important body functions[5].

In its commercial packaging[*)] the drug is combined with high doses of vitamins B_1, B_6 and B_{12}, whose antineuritic and antalgesic action is well known, and with diisopropylammonium dichloroethanoate, a substance which may have the ability to ensure that tissues are in the best possible condition to be able to use the energy obtained from oxidative phenomena, probably by encouraging recoupling of oxidising reactions with processes of phosphorylation[1, 6]. In previous tests conducted on animals this pharmacological combination has proved to be particularly useful since the product has demonstrated that it possesses an antiphlogistic and antalgesic action clearly superior to that of the individual constituents taken separately, a phenomenon which can be explained by the existence of phenomena of positive synergy between the various constituents of this product[5].

On the basis of these clinical results we decided to use this drug to treat a certain number of patients with rheumatic diseases of various kinds, studying its therapeutic effect and general tolerance over lengthy periods of administration.

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[a] Translator's note: no English trademark could be found for this product.

[*)] "Menalgon Antireumatico" from Laboratori Farmaceutici Menarini – Florence

Equipment and method

Our study was conducted on 50 patients, aged between 19 and 78 years, suffering from various types of rheumatic disease of different etiology. Given the heterogeneity of the case history, it seemed advisable to follow a nosographical criterion, subdividing into the following groups:

1) group of subjects suffering from osteoarthrosis in various locations, comprising a total of 37 patients. The main location of the disease related to the lumbar-sacral section of the spine in 11 cases, knee joints in 9 cases, the cervical section of the spine in 6 cases, scapulohumeral joints in 3 cases and tibiotarsal and tarsometatarsal joints in 2 cases. In all patients the X-ray examination of the regions concerned showed a reduction in joint spaces, presence of osteophytes, thickening of the subchondral bone and areas of osteoporosis. In some patients suffering from vertebral osteoarthrosis clinical symptoms were accompanied by radicular effects consequent on disc disease (brachialgia or sciatica). Erythrocyte sedimentation rate and rheumatic activity tests (antistreptolysin titer, C-reactive protein, lattice test, Waaler-Rose reaction, uricaemia, mucoprotein, serum protein electrophoresis) were in all cases within normal limits;

2) group of cases of acute periarthritis based in the scapulohumeral and pre-rotulian area, involving 5 patients. In these cases the disease was characterised by intense pain, periarticular swelling and functional impotence. In three cases X-rays revealed juxta-articular calcification (located in the supraspinal area and in the femoral quadriceps). Serological tests were normal in three cases, while the remaining two revealed a slight increase in ESR and the hemochromocytometric examination showed a certain level of neutrophilia;

3) group of cases of acute segmentary myositis in the cervical or lumbar region, including three cases in which the inflammatory process was attributable to factors of a physical type (chilling). The X-ray examinations and rheumatic activity tests, carried out in all cases, always produced normal results;

4) group of cases of neuritis and polyneuritis at various pathogenetic points, including 4 patients whose serological and radiological data were within normal values at all times;

5) we also submitted for treatment one case of rheumatoid arthritis in its initial phase ("probable" according to ARA criteria)[3] in which slightly painful symptomatology was present with a feeling of morning stiffness located in the hands and wrists, a slight increase in ESR and a serological report negative for the rheumatic factor (lattice test and Waaler-Rose reaction).

In all our patients the preparation was administered in coated tablets containing 200 mg of o-ethoxy-benzylhydrazone of diethanolamine pyruvate, 20 mg of di-isopropylammonium dichloroethanoate, 50 mg of vitamin B_1, 50 mg of vitamin B_6 and 500 mg of vitamin B_{12}. The initial dose was 3-6 tablets per day, subdivided into three doses over periods of varying duration (from 7 to 20 days), depending on the clinical progress of the disease and individual tolerance. We performed numerous tests in all patients at the start, during and at the end of treatment, aimed at identifying any impairment of the functions of the most important organs and systems which might have been induced by the drug. For this reason we checked hematic crasis, hepatic, renal and gastric function and finally cardiovascular function, using the following tests: hemochromocytometric test, prothrombin time, serum colloidal tests, bilirubinaemia, transaminases, alkaline and acid phosphatases, serum protein electrophoresis trace, full urine test, spontaneous fractionation, concentration test, dilution test, azotemia, glycaemia, electrocardiogram, blood cholesterol, search for faecal occult blood. At the beginning and end of treatment we also carried out an X-ray of the stomach and duodenum in order to check for the pre-existence or onset of any impairment to organs or functions within the gastroduodenal tract.

With regard to the therapeutic efficacy of the preparation, this was evaluated by taking into consideration its analgesic and anti-inflammatory action which, as already pointed out, had been previously documented in experimental tests on animals. To this end we evaluated, in particular, pain symptoms and resumption of joint function in the sites affected by the disease. We also

noted particular effects which occurred and were observed in certain patients or groups of patients. More specifically, in the only case of rheumatoid arthritis observed, presenting an initial involvement of joints in the hands and wrists, we evaluated the duration of morning stiffness and repeatedly, over the treatment period, checked the strength of the parts involved using ordinary dynamometric tests.

The results obtained were considered *excellent* when after a few days of treatment we noted complete regression of painful symptomatology and signs of phlogosis in all the areas concerned, with complete resumption of functions in the areas involved. We considered the results to be *good* if, although pain had disappeared and the signs of phlogosis had reduced, resumption of functions was still incomplete. However results of those cases in which we noted only a reduction or disappearance of the symptoms of pain were classified as *fair*. The therapeutic result in which symptomatology remained unchanged and only minimum effects of the treatment were felt in spite of continuous administration of the drug over a lengthy period of time was considered *useless*.

Results

The individual and overall results obtained in our case history are shown in tables 1 and 2. On the basis of the data recorded, we should first of all point out that in none of the cases we treated was it possible to show considerable or in any event significant changes in the various examinations and functional tests carried out. In particular the tests on kidney, liver and heart function always proved to be normal. Under no circumstances did we note any changes in hematic crasis falling outside normal limits. In terms of gastric tolerance, this can undoubtedly be considered good, since in no case were we obliged to halt treatment on account of the onset of side effects, such as feelings of heaviness, gastralgia, pyrosis, and gastric acidity (although this frequently occurs with other antirheumatic preparations commonly used in treatment. Only two patients (table 1 n° 12 and n° 39) presented a slight and completely temporary problem represented by a feeling of heaviness in the epigastric area and slight gastric pyrosis, respectively. X-rays of the stomach and duodenum, carried out before and after treatment, did not show damage to the gastric or duodenal wall in any patients. In addition the faecal examination, carried out periodically, never showed the presence of occult blood which might suggest the onset of erosion or ulceration at gastric or duodenal level. With regard to other undesirable side-effects, none of the cases treated presented any skin rash, headache or other problems.

The analgesic action of the preparation was noted in almost all patients, as can be seen from table 1, being particularly evident not only for neuritis and polyneuritis and segmentary myositis, but also in osteoarthrosis of varied location. Above all it seems worthy of note to emphasise how in a considerable number of cases of arthritis in the cervical, lumbar-sacral, scapulohumeral, coxofemoral and tibiotarsal areas, and in the knee, the drug was able to obtain good, and often extremely successful results; the improvement was characterised by a clear reduction in pain and feeling of stiffness in the joints, and in many cases this was supported by the objective observation of an increase, sometimes fairly good, in joint mobility. These results are of particular practical interest since some of these locations (such as for example the lumbar-sacral and coxofemoral area) are notorious for being amongst the locations of arthritic disease which are the most difficult to influence significantly using the medical and physical treatment resources currently available[3].

The preparation also produced good results in cases of painful radicular syndromes consequent on arthritic lesions in the vertebrae and the expression of a disc-radicular conflict, especially in those cases in which the phlogistic component, the cause of radicular pain, was particularly marked and dominated the mechanical-compressive factor.

TABLE 1

Case n°	Age (yrs)	Sex	Clinical diagnosis	Dosage	Clinical effect	Side effects
1	52	M	Lumbar-sacral arthritis	2 tab X 3	Good	-
2	57	M	Lumbar-sacral arthritis with sciatica	2 tab x 3	Good	-
3	72	F	Lumbar-sacral arthritis with sciatica	2 tab x 3	Good	-
4	71	M	Lumbar-sacral arthritis with sciatica	2 tab x 3	Excellent	-
5	46	F	Lumbar-sacral arthritis with sciatica	2 tab x 3	Good	-
6	44	M	Lumbar-sacral arthritis with sciatica	2 tab x 3	Good	-
7	56	M	Lumbar-sacral arthritis	1 tab x 3	Good	-
8	78	M	Lumbar-sacral arthritis	1 tab x 3	Good	-
9	67	M	Lumbar-sacral arthritis	2 tab x 3	Good	-
10	55	M	Lumbar-sacral arthritis	2 tab x 3	Good	-
11	44	F	Lumbar-sacral arthritis	2 tab x 3	Fair	-
12	68	M	Knee arthritis	2 tab x 3	Good	Epigastric heaviness
13	60	F	Knee arthritis	1 tab x 3	Good	-
14	75	M	Knee arthritis	2 tab x 3	Fair	-
15	73	F	Knee arthritis	2 tab x 3	Good	-
16	68	M	Knee arthritis	1 tab x 3	Good	-
17	63	F	Knee arthritis	2 tab x 3	Fair	-
18	58	F	Knee arthritis	2 tab x 3	Fair	-
19	65	F	Knee arthritis	2 tab x 3	Good	-
20	72	M	Knee arthritis	2 tab x 3	Good	-
21	48	M	Cervical arthritis with brachialgia	2 tab x 3	Excellent	-
22	65	F	Cervical arthritis with brachialgia	1 tab x 3	Excellent	-
23	37	M	Cervical arthritis with brachialgia	2 tab x 3	Excellent	-
24	51	F	Cervical arthritis	2 tab x 3	Good	
25	65	F	Cervical arthritis	2 tab x 3	Fair	-
26	67	F	Cervical arthritis	2 tab x 3	Good	-
27	45	F	Coxofemoral arthritis	2 tab x 3	Good	-
28	68	M	Coxofemoral arthritis	2 tab x 3	Good	-
29	51	M	Coxofemoral arthritis	2 tab x 3	Good	-
30	64	F	Coxofemoral arthritis	2 tab x 3	Fair	-
31	65	F	Coxofemoral arthritis	2 tab x 3	Fair	-
32	57	M	Coxofemoral arthritis	2 tab x 3	Good	-
33	42	M	Scapulohumeral arthritis	2 tab x 3	Good	-
34	38	F	Scapulohumeral arthritis	2 tab x 3	Fair	-
35	62	F	Scapulohumeral arthritis	2 tab x 3	Good	-
36	53	M	Tibiotarsal arthritis	1 tab x 3	Good	-
37	42	M	Tibiotarsal arthritis	2 tab x 3	Fair	-
38	60	M	Scapulohumeral periarthritis	2 tab x 3	Fair	-
39	47	F	Scapulohumeral periarthritis	2 tab x 3	Good	Mild gastric pyrosis
40	56	F	Scapulohumeral periarthritis	2 tab x 3	Fair	-
41	34	M	Scapulohumeral periarthritis	2 tab x 3	Good	-
42	51	F	Knee periarthritis	2 tab x 3	Fair	-
43	19	M	Cervical myositis	1 tab x 3	Excellent	-
44	31	M	Lumbar-sacral myositis	2 tab x 3	Good	-
45	25	M	Lumbar-sacral myositis	2 tab x 3	Good	-
46	70	F	Herpes zoster	2 tab x 3	Good	-
47	42	M	Polyneuritis (in alcoholic subject)	2 tab x 3	Good	-
48	44	M	Post-traumatic intercostal neuritis	2 tab x 3	Good	-
49	25	F	Trigeminal hyperalgic syndrome	2 tab x 3	Good	-
50	38	F	Rheumatoid arthritis	2 tab x 3	Good	-

As mentioned above, the drug also proved to be effective in patients suffering from neuritis or polyneuritis, of varying types of etiology, or in whom there was objective evidence of painful segmentary myositis.

In subjects in whom the existence of symptoms of periarthritis (scapulohumeral or knee), the drug seems to have had less therapeutic efficacy, even if a definitive opinion is difficult to pronounce, given the limited number of clinical case histories.

TABLE 2 - *Overall therapeutic results obtained in 50 patients.*

Result	Number of cases	%
Excellent	5	10
Good	32	64
Fair	13	26
Useless	-	-

With regard to the only case of rheumatoid arthritis treated we achieved good results, in the form of regression of painful symptomatology and morning stiffness and with ESR returning to normal values. We should bear in mind that this was a case of initial rheumatoid arthritis (*probable* according to ARA criteria) therefore, taking into account the fact that this also concerned one single case rather than a sizeable group of patients, expressing any certain therapeutic opinion seemed to us clearly premature. It will undoubtedly be interesting to observe the effects produced by the drug on an extensive case history and in particular in the *definite* or *classic* forms of rheumatoid arthritis, especially if these date back several years and have already received protracted steroid treatment, in order to check the action of the drug administered on its own or combined with steroids, with synthetic antimalarics, etc, and to demonstrate any potentiating and/or sparing action on these substances, a situation well known to be extremely useful in the protracted treatment of rheumatoid patients.

When the drug produced useful effects these always took place at a fairly early stage, and were already present on the first day or days of treatment. This effect is of a "suspensive" type since in general it regresses rapidly when treatment is halted. More specifically we were able to note that the action of the preparation usually occurred between 1 and 2 hours after administration and lasted for a time period of between 8 and 9 hours. We therefore consider that in order to obtain a good therapeutic effect and to cover the patient throughout the 24 hour period, fractionated administration of the preparation is required, with a single dose every 7 to 8 hours.

It also seemed advisable to stress that in some patients in our case history and in particular in older patients and those who had been suffering from the disease for a longer period, the drug demonstrated a general trophic action, probably due to the high doses of vitamins contained in the preparation which can stimulate overall metabolic activity and produce an antiasthenic action on symptoms such as asthenia and adynamia, which frequently occur in rheumatic forms and are probably connected with multiple vitamin deficiencies and a state of functional corticoadrenal insufficiency.

Conclusions

In our study we treated 50 patients suffering from various types of rheumatic disease with a new synthetic drug, o-ethoxy-benzoylhydrazone of pyruvic acid, in order to establish its pharmacological action in the various types of arthropathy as well as the tolerability of the product over long periods of treatment. It can be seen from all the observations that the drug we used possesses intense analgesic and anti-inflammatory activity and therefore can be indicated for the treatment of many types of rheumatic disease. The results obtained allow us to state that the preparation is undoubtedly useful in the treatment of many cases of osteoarthrosis. The effect is that of clear regression of painful symptomatology, frequently accompanied by a reduction in functional impotence, together with an improvement in joint function. With regard to the mechanisms by means of which antiphlogistic and analgesic action take place (better than that of acetosalicylic acid and aminopyrine) it is necessary to bear in mind the extreme complexity of interpreting the *phenomenon of phlogosis*. Although, in fact, the knowledge of the pathogenetic

mechanism of inflammation has now made substantial progress, new prospects for exploration have nevertheless emerged, as well as new questions to be answered. We might mention the problems associated with studying vascular changes in the preinflammatory phase and the information available, for example, on the role of plasma quinine in the inflammatory response[7]. In addition nonsteroid anti-inflammatory substances (including the drug we used) constitute a group which is extremely heterogeneous from both a chemical and pharmacological point of view: indeed their structures are diverse and their pharmacological activity varied, since they can act on one or more elements of phlogosis, on edema, pain or granulation tissue, without it being possible to predict this diverse activity from their chemical composition[2]. If we consider the results of the clinical research, it seems interesting to point out that the antiphlogistic effect of our drug was evaluated by calculating the inhibition of local edema caused by substances such as formalin, dextrane and bradikynin. The clear antiphlogistic effect was also ascertained by taking into account a generalised edematous reaction, known as anaphylactoid oedema elicited by egg white in the rat: this experimental picture can be largely traced back to histamine-induced pathogenesis[4]. However, as with like dextrane-induced oedema, it is also associated with phenomena of hypersensitivity inherent in the receptor tissues[5].

Nor should we ignore the analgesic action produced by vitamin B_1, vitamin B_6 and vitamin B_{12}, through direct tropism on the metabolism of nerve fibres and on neuron sheath components. Experimental pharmacology has in fact shown that a deficiency in these vitamins is accompanied by processes of lipolysis and by the mobilisation of myelinic fatty acids, by local acidosis and by increased acetylcholinesterase activity, all phenomena which induce the local pathological situations responsible for neurogenous hyperalgesia[2]. This mechanism, therefore, may also explain the favourable effect produced by the drug on forms of neuritis, polyneuritis and segmentary myositis.

In all the cases treated the preparation was well tolerated even after long periods of administration: indeed at no time did we note in any of our patients the onset of the type of side-effects which often oblige the rheumatologist to halt treatment.

Repeated laboratory tests carried out in order to check the effect of the drug on the functions of various systems at no time revealed the onset of impairment or lesions to suggest that the drug has a damaging effect on the tissues or functions of any organ. On the contrary we can state that the product we used showed that, alongside absolute tolerability, it possesses an antiasthenic and general eutrophic effect which overall give it an undoubted advantage in comparison with other antirheumatic drugs. The preparation should therefore be ranked alongside other antiphlogistic drugs with a "suspensive" action. Consequently its therapeutic indications are essentially associated with diseases for which therapy with anti-inflammatory drugs with "suspensive" action is indicated.

In conclusion, therefore, we can state that this new preparation, by virtue of its clear antiphlogistic and analgesic action, its excellent tolerability and the absence of undesirable side-effects, even after long periods of treatment, represents a product of undoubted interest from a theoretical point of view and of advantageous practical application in terms of treatment.

SUMMARY

Medical Clinic (*Director Prof. R. Marcolongo, University of Siena*)

G. Blanco, R. Marcolongo, N. Di Paolo: Clinical results with a new synthetic preparation in the treatment of rheumatic disease. The Authors studied the antirheumatic action of a new anti-inflammatory drug (o-ethoxy-benzoylhydrazone of pyruvic acid), commercially prepared in association with high doses of vitamins B_1, B_6, and B_{12}. The clinical experiment involved 50 cases of rheumatic disease (37 osteoarthrosis, 5 acute periarthritis, 3 myositis, 4 neuritis and 1 initial rheumatoid arthritis). Excellent tolerance was noted even in the case of extremely protracted treatment and no significant side-effects were observed. Excellent and good anti-inflammatory and antalgesic effects were noted in 10% and 64% of the series respectively. Attention is drawn to the early action of the drug, benefit being felt in the first days of treatment in many cases. A general trophic and anti-asthenic action was noted in all subjects in the series. The new

association is indicated as a valuable aid in the management of rheumatic disease

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Expenditure of energy and nutrition of horses during effort

Race horse dietetics

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Summary – The optimum food balance for race horses is mainly characterised by: a sufficient level of cellulose (≥ 13-15%), quite a large but controlled share of nitrogen-free extract (starch), a supplemented intake of essential fatty acids (oils), a limitation of the protein content (towards 11-12%), increased supplementation of calcium, salt and trace elements, liberal supplementation of vitamin E and vitamin [*B*] complexes, and the possible use, after much consideration, of ergogenic nutritional factors well proven for their innocuousness and effectiveness.

Race horse/food balance/health/performance/ergogenic factors

Introduction

Horses are exceptional athletes, strictly selected over a very long time by nature, then by man, to become strong sprinters, with the most brilliant sporting potential. Yet their food rationing is generally attached to simplistic traditions, unsuited to high performance levels and especially to repeatability and durability. Consequently, it is not surprising that there are many disappointments, in rearing and training, such as "growth crisis", lack of precocity, bone and tendon accidents, lack of stamina in races, early and persistent fatigue .... These different handicaps lead to unavailability which prevents the conduct of intensive, well-programmed training. They make the frequent and improper use of different palliatives, expedients, anti-inflammatories, stimulants and different medicines overly attractive. They seriously harm the horse's career, the owner's, trainer's and enthusiast's satisfaction and the profitability of horse speculation. Furthermore, they hinder selection and may even lead to deselection since the best horses risk being the first and most harshly affected and are then eliminated from competition and reproduction prematurely. Thus, in the United States, out of every ten thoroughbred foals, five reach the race course and only one is kept in competition after the first year of training. Moreover, it is striking to note that, unlike sportsmen and women who never cease beating their records, race horses improve their maximum performance very little, despite the most rigorous selection and the highest financial incentives. For example, since 1900 the speed of the Epsom Derby has increased only by 2%. More generally, the times of the winners of the main races have changed very little over the last fifty years.

Modern knowledge of equine nutrition to date has led to consistently excellent zootechnical results (Wolter, 1975a-1975b; Jarrige et Martin-Rosset, 1984), while minimising the multiple conditions triggered or promoted by mistakes with food, such as colic, founder, myopathy, osteotendinous problems, infertility, etc (Wolter, 1973, 1979, 1980, 1981, 1983a, 1983b, 1987, 1991a, 1991b and 1992).

The way muscle works very directly influences the type of energy requirements. It, therefore, has an effect on the optimal choice of food energy sources and on all the characteristics of the best nutritional balance.

Energy sources and balance in the ration

The harder and more sustained the work, the more important it is to prepare rations with a high energy concentration, which can easily meet the requirements, without having to multiply the number of meals and without overloading the digestive system. While cellulose essentially plays the role of bulk, still essential for digestive hygiene, nitrogen-free extract retains a major place in the sprinter's intake. However, for long-distance runners, increased use of lipids is favourable for aerobic work, in addition to the beneficial effect of essential fatty acids with regard to aptitude for sport.

Cellulose

It is a very mediocre source of energy, especially as it is more polymerised and lignified. Less well digested than nitrogen-free extract, it only breaks down into volatile fatty acids which have a low energy yield even if they do not risk causing problems with ketosis. However, a minimum rate of 15% is necessary to stimulate digestive transit in the large intestine and thereby to prevent stases and dysbacteria which cause colic, founder, and auto-intoxication which harm the physical form and may even predispose to muscle problems.

Nitrogen-free extract

It has a relatively liberal place in race horses where it constitutes the main source of energy in the form of cereals, specifically oats, the proportion of which in the ration increases with the amount of work while the share of fodder regresses. However, it has both digestive and metabolic limits.

Digestion

Starch has the advantage of being mainly digested early in the small intestine, into glucose which has a much better energy yield than volatile fatty acids. However, amylasic activity is quite restricted in horses (Roberts, 1974). Therefore, too sudden, too abundant or insufficiently fractionated intake of cereals risks overwhelming the enzyme digestion abilities in the small intestine and providing a substrate too overly prone to fermentation in the microflora of the large intestine. The result of this is that, in addition to a loss of yield, digestive acidulosis responsible for intestinal inflammation ("burned intestine"), dysbacteria with the complications mentioned before, related to the overload of lactic acid, into amines such as histamine, or even endotoxins.

Prevention is based firstly on the capping of the daily ration of cereals, too often excessive because energy expenditure tends to be overestimated, while excess weight is the first handicap vis-à-vis sporting performance. It is also appropriate to recommend many small

meals to make up the daily allocation of cereals; it should be remembered that the "Compagnie des petites voitures de Paris" provided for eight to ten meals a day in 1890. Without reaching that demanding frequency of manpower, a minimum of three meals of concentrate per day appears desirable in horses working intensively, in order to regularise the digestive transit and facilitate digestion. The crushing or grinding of grains can also become favourable with a high level of food. Hydrothermal treatments of flaking or expansion-extrusion, which gelatinise the starch, are even likely to be profitable provided they do not lead to untimely gastric fermentation or metabolic overload.

Metabolism

As we have already stressed, nitrogen-free extract can exaggerate the storage of glycogen in the muscle and promote its anaerobic catabolism, encouraging dangerous overproduction of lactic acid. That then predisposes to acute rhabdomyolysis, especially while working after a rest, during which the allocation of grain or other concentrates has not been sufficiently reduced ("Easter Tuesday disease"). It is, therefore, important to adjust the amylase intake overall to the energy requirements at the time, while ensuring a good supply of B complex vitamins and vitamin E and selenium with a view to better prevention of strokes. When very long effort is planned with exposure to exhaustion of glycogen reserves in the muscle, it is actually more sensible to adapt the horse in advance to a diet enriched in fats, rather than exaggerating the supply of nitrogen-free extract. Furthermore, before effort, it is necessary to prohibit the distribution of very quickly absorbed sugar which leads, through hyperinsulinaemia, to secondary hypoglycaemia, which is contrary to performance. Thus, glucose as a food intake before exercise can alter performance (Hardgreaves [*sic*] et al, 1985), while during long and intense effort, it contributes to maintaining glycaemia and delaying fatigue. In pre-exercise, fructose appears preferable because it is less hyperglycaemic than glucose or bread starch or mashed potato (Guezennec et al, 1989) such as amylase compared with amylopectin (Guezennec, 1989). Before and during prolonged effort, the best results in sports men and women, probably valid in horses, are to date guaranteed by glucose polymers or maltodextrins, alone or in combination with a lesser proportion of fructose (Costill, 1988; Coggan and Coyle, 1989; Coyle, 1989, Ryan et al, 1989; Brown et al, 1989).

Lipids

These are excellent sources of energy for endurance trials in aerobiosis (Wolter et al, 1983). This is because, even in horses, they cumulate the advantages of good acceptability and high digestibility (Bowman et al, 19077; Hintz et al, 1978; Kane et al, 1979; Hambleton et al, 1980; Wolter and Valette, 1985). Furthermore, they have the merit of a high energy concentration (2.35 times that of proteins or nitrogen-free extract).

In horses, which are generally sprinters rich in rapid muscle fibres, trained for short and intense efforts, food lipids often have only a restricted place. But in horses which undergo endurance efforts, they are likely to improve performance by allowing a saving of muscle glycogen and great stability of glycaemia; several authors have reported this: Slade et al (1975) with the addition of 9% maize oil in the diet of horses running a 67 km race; Hintz et al (1978) thanks to the addition of 8% of animal fat in the ration of thoroughbreds running 60 km, or Arabs running 83 km at 15 km/h; Hambleton et al (1980) adding up to 16% maize oil in horses running a long-distance of 67 km. Harkins et al (1992) also improve the sporting performance of race horses thanks to the addition of maize oil to food; that increases the

muscle content of glycogen at rest and after effort (the latter aspect is questioned by Scott et al, 1992). In the same way, our tests (Wolter and Valette, 1985) have shown excellent effectiveness of lard, but also a certain superiority of a mixture of lard (1/2), coconut fat (1/4), sunflower oil (1/4). This is because it is necessary to stress the particular advantages:

- of medium-chain fatty acids which are more easily digested, even in the event of biliary insufficiency (where there are lower faecal losses of calcium and magnesium), which are more easily carried in the body (without risk of hepatic steatosis) and which are preferentially metabolised without requiring the availability of carnitine, which is essential for the intramitochondrial transfer of long fatty acids;
- essential fatty acids (EFAs) which enter the constitution of the biological membranes. Their polyunsaturation increases membrane permeability and, thereby, the intensity of the energy metabolism and the aptitude for sport.

Furthermore, our laboratory (Valette, 1984; Wolter et al, 1984) has also highlighted the value in supplements containing magnesium in order to prevent any hypomagnesaemia likely to be promoted by hyper fatty diets (faecal losses of magnesium soaps) and through muscle work (increased losses in urine and sweat). Our studies, according to an adapted methodology (Wolter et al, 1984) related to the potentialising effect of a metabolic carrier of fatty acids: carnitine.

Of course, these hyper fatty diets must be rebalanced totally to take into account their strong energy concentration. They must also be very anti-oxidated and supplemented with the vitamins involved in the metabolism of fatty acids. Finally, it is necessary to ensure a gradual introduction through a transition over one to two weeks.

Proteins

The work of muscles would modify slightly the level of protein requirements since it essentially consumes "empty calories" and preserves tissue proteins as much as possible. To the extent that it is moderated, it tends to increase nitrogen retention (Freeman et al, 1988); on the contrary, if it is very intense or very prolonged, it strengthens nitrogen catabolism. The requirements might be increased sometimes from 25 to 100% in sportsmen and women (Pérès, 1990) and without doubt in horses too. The protein level could theoretically be reduced as the energy requirements progress; however, an underlying protein deficiency promotes the appearance of "sports anaemia". Now, physical activity already leads to a certain increased wear and tear of the "animal machine" which probably leads to some increase in nitrogen requirements. That is even more marked at the start of training during the build-up of muscle. Above all, protein intakes must be clearly strengthened the more intense the stress, linked to the severity of the training and/or the psychological stress of competition. That stimulation of nitrogen catabolism in relation to the work of muscles is particularly sensitive in very intense or very long effort where it leads to a strong rise in blood urea, uric acid and creatinine levels (Luke and Hall, 1980; Snow et al, 1982; Green and Fraser, 1988; Friedman and Lemon, 1989), and a much larger urinary excretion of methylhistidine (Hickson and Hinkelmann, 1985). With regard to this, one specific metabolic feature of the horse should be emphasized which, compared with other species, protects its muscle nucleotides better by limiting their degradation into uric acid. On the contrary, it stimulates desamination of AMP (derivative of ATP via ADP) into IMP (inosine monophosphate); the ammonia released at that time activates glycolysis which benefits rapid effort (Cutmore et al, 1986), but over a short period as it stimulates the accumulation of lactic acid.

Yet, it is also necessary to avoid excess nitrogen. This is because firstly it increases exposure to putrefying dysbacteria in the large intestine with a change in the quality of the faecal matter and to a certain risk of chronic auto-intoxication. Furthermore, the proteins reabsorbed in excess have a mediocre energy yield; they also lead to nitrogen waste which overloads the liver and kidneys again and which hinder the mechanism of the Krebs cycle. This is because hyperammoniaemia hinders the carboxylation of pyruvic acid, dehydrogenation of citric acid, the availability of ketoglutaric acid (captured to form glutamic acid and glutamine); it, therefore, causes an accumulation of lactate and a reduction of the supply of ATP and would go hand in hand with a state of fatigue (Miller and Lawrence, 1986). That would also be promoted by metabolic acidosis resulting from exaggerated lipolysis (free fatty acids and β-hydroxybutyric acid) in relation to hyperprotein diets (Maugham, 1989). At the very least nitrogen overloads raise ammoniaemia, exaggerate sweating, stimulate diuresis and therefore increase water requirements (Slade et al, 1975). Furthermore, sporting performance risks being reduced (Mutch and Banniter, 1983). Thus, according to Glade (1983), an excess of 1,000g of total nitrogen matter, compared with the standards of the National Research Council would increase the race times by 1 to 3 seconds over distances of 1,200 to 1,700 m. However, this negative effect of a protein overload (24% instead of 12% in the ration) is not found in endurance races by Hintz (1983); in the same way, a protein level of 18.5% compared with 12.9% does not reveal harmful consequences in horses trained on a treadmill (Miller and Lawrence, 1988).

Practically, the protein level of the race horse's ration will therefore remain on average close to 11% (Hintz, 1985) and in sprinters, more exposed to the stresses of competition, and in long-distance runners whose ration can be enriched with fats. Where required, the protein quality will be improved by using alfalfa flours, soya cake, etc.

Minerals

The repercussions of the work of the muscle are particularly clear for the sodium chloride, and calcium and magnesium requirements, but they also relate to trace elements.

Sodium chloride

It is exported abundantly by sweating which is dependent on the intensity of the effort and its length, the level of training (at the start the sweat is more diluted and secreted in excess) and climate conditions. It would improve resistance to fatigue and even to rhabdomyolysis (Harris et al, 1988 in: Snow and Harris, 1989). The requirements may increase up to 50 to 70 g/d. They are covered by food levels of the order of 0.5%. Furthermore, the free availability of salt lick allows for self-regulation in the medium- and long-term, but it is necessary to avoid initial overconsumption which can lead to diarrhoea, while stones which are too hard or too rare may lead to under-consumption. In the short-term, the addition of salt to drinking water is even beneficial, after an exhausting effort, in order to restore volaemia quickly without increasing the hypo-ionia from hyperionic losses in sweat: for example up to 20 grams of salt in 20 litres of warm water distributed intermittently to prevent water colic before allowing free access to pure water. A potassium supplement is also desirable to combat fatigue and muscle weakness.

One can easily conceive of more elaborate rehydrating preparations, with a view to strengthening resistance to fatigue and accelerating recovery during or following competition.

With regard to this, it should not be forgotten that fast trials lead to metabolic acidosis because of overproduction of lactic acid in the muscles, while very long trials in strong heat expose more to alkalosis because of the large losses of chloride in sweat rather than sodium and potassium, and calcium and magnesium (Arghi et al, 19845). In endurance trials, one could thus provide at least every two hours for the distribution of approximately 5 litres of an electrolytes solution, containing chlorine, sodium, potassium, calcium and magnesium, not forgetting to have additional drinking water freely available.

Calcium and magnesium

It is also worth increasing the amount of calcium and magnesium in the race horse's ration. Calcium prevents osteofibrosis in sportsmen and women, with joint pain and fragility of the skeleton. Magnesium prevents laxity of the tendons. Both contribute, as stimulants of the central nervous system and moderators of the peripheral nervous system, to obviating hyperexcitability with nervous predisposition, myoclony, tetany, etc., while maintaining very good neuromuscular tone.

The digestibility of these two macro-elements may already be changed by diets rich in saturated fats which promote the formation of insoluble soaps. Their retention is also reduced by lactic acidosis, which exaggerates their loss in urine and reduces the metabolic effectiveness of vitamin D, which would also be slightly reduced by protein excesses which increase urinary excretion of sulphate (Glade et al, 1985). Furthermore, tissue lipolysis, used to best effect during endurance efforts, contributes to fixing magnesium in the adipose tissue and to multiplying the risks of hypomagnesaemia and even hypocalcaemia (Rayssiguier, 1977).

Above all, the digestibility and retention of calcium, and of magnesium, are seriously compromised in race horses by the usual food excesses of total phosphorus and by the phytic form of the latter. This is because as the level of work increases, cereals, in particular oats, take an increasing place in the ration, to the detriment of hay. They, therefore, gradually impose their phosphocalcic imbalance with their Ca/P ratio of the order of 0.2-0.3 in comparison with an optimum close to 1.5. Furthermore, the phytic form of two-thirds of their phosphorus hinders the reabsorption of the calcium and also of the magnesium and even of trace elements such as zinc, by forming insoluble phytates in the small intestine; these are then found dissociated by the microflora of the large intestine at which level the phosphorus released may still be absorbed, unlike the minerals it had previously blocked. Excessive phosphorous therefore results in aggravated hyperphosphataemia, which is responsible for hyperparathyroidism. Adding to the sensitivisation caused by chronic acidosis which can be derived from the work of muscles, this leads to bone demineralisation corresponding to osteofibrosis which takes account of the particular fragility of the bone and tendinous tissue in race or sports horses. This may explain the frequency of osteoarticular and tendinous problems with names and manifestations as diverse as "growth crisis", "bone disease", "epiphysitis", "osteitis", demineralisation predisposing to skeletal pains, lameness in various places but causing repeated unavailability which disturb training, lower performance, curtails careers.

Prevention is consequently especially important. It clearly requires increasing calcium intakes, well beyond the traditional recommendations, up to 0.7-0.8% of the intake, looking for a Ca/P

ratio greater than 1.5. In the same way, it is appropriate to increase the supply of magnesium to reach nearly 0.15% of the intake. When required, it is also useful for combating metabolic acidosis. It is still necessary to avoid any excess of vitamin D which can only precipitate the installation of osteofibrosis and make it more irreversible.

Trace elements
They generally gain by being present in double proportions, compared with the minimum standards, to increase the safety margins, take account of the progression of the energy concentration, to counteract the reduction of their rate of assimilation resulting from the antagonist effect of the calcium overload. Furthermore, some of them are of particular value.

Iron: Enters into the composition of haemoglobin and myoglobin. Its assimilation would be more or less reduced by excess phosphorus. However, deficiency is not very likely in view of the great richness of the fodder. Overloads, specifically in organic form, would therefore have only a transitory effect, even by potentialising them with supplements of copper and vitamins Bc and B12.

Copper: Participates in erythropoiesis by facilitating the metabolic use of iron. Furthermore, it contributes to the strength of bones, cartilage and large blood vessels by conditioning the synthesis of collagen and elastin; in particular, it contributes to the prevention of osteochondrosis, unlike its antagonist, zinc. The usual imbalance in fodder justifies systematic supplementation, as for zinc.

Zinc: Already not very well represented in most fodder, it is also poorly assimilated in the presence of high levels of phytates and/or of calcium. Furthermore, the work of muscles increases its loss in sweat and urine. It would improve resistance to fatigue, perhaps through its role as cofactor of lactodehydrogenase.

Iodine: Activates thyroid function; it promotes bone development; it might even intervene in the prevention of myodystrophies, although selenium is then the element of choice; but excess iodine (beyond 3 to 5 ppm) leads to the birth of weak and goitrous foals.

Selenium: In combination with vitamin E, it prevents the oxidation of polyunsaturated fatty acids constituting the cell and sub-cell membranes and therefore guarantees their integrity, especially at muscle level. The primary deficiency, responsible for myodegeneration, has already been described for horses (Wilson et al, 1976). Furthermore, the requirements are increased during work, especially if it is accompanied by overproduction of lactic acid which compromises resistance of sarcolemma and intramuscular oxygenation. They are also increased parallel to the proportion of unsaturated acids in food. In practice, the subclinical deficit of selenium seems to change the horse's aptitude for sport (Blackmore et al, 1979).

Chromium It is necessary for hepatic proteosynthesis and the activity of glycogen-synthetase (Campbell et al, 1989).

Vitamins

Vitamins are also recommended at higher rates, without reaching excesses which give exposure to serious hypervitaminosis with fat-soluble factors or wasting with water-soluble factor (Wolter, 1983).

Of the fat-soluble factors, the intakes in comparison with the basic standards can be nearly doubled for vitamins A, D, K and even tripled for vitamin E if the ration is widely provided with unsaturated fatty acids. But massive doses have generally been found to be ineffective for increasing sporting performance while they are not without risk.

Vitamin E has attracted much attention because of its anti-inflammatory properties compared with histamine and acetylcholine (Kamimura, 1972) and because of its especially important antioxidant property in this case since physical exercise stimulates lipidic peroxydation (Vinicka, 1984), although Sharman et al (1971) observe that an overload of vitamin E has no effect on sporting performances. Lingholm and Asheim (1973) grant it a positive action. In high doses, vitamin E would protect erythrocytes and would increase hematocrit (Lawrence and Slade, 1979); it would contribute to fighting against degenerative myeloencephalopathy.

Roneus et al (1986) place the optimum intake in standard breeds between 600 and 1,800 mg of Dlα-tocopherol per day; in the same way, Schubert (1987) finds that the 1,000 mg dose of vitamin E per horse and per day tends to increase the chances of success. In humans, in mountain sports, supplements of 400 mg per day would improve performance (Simon-Schnass, 1988).

Misuse of vitamin D (towards 10 to 100 times the nutritional recommendations), especially in the form of D_3 more dangerous than D_2, depresses the appetite, changes the general condition, leads to lameness and above all causes serious calcifications of the large blood vessels while the skeleton demineralises. The legislator wisely limits the level of incorporation of vitamin D (D_2 or D_3) to 4,000 UI/kg of intake.

Overloads of vitamin K, in the vain hope of preventing nose bleeds in race horses (these are in fact pulmonary haemorrhages linked to very intense effort) expose to kidney problems with haematuria and hyperuraemia.

The different water-soluble factors are more or less directly favourable to cellular oxidation and the work of the muscle. Compared with the usual recommendations, the supplements are likely to be clearly increased through a simple concern for safety because it has not been proven that horses can suffer deficiencies. On the other hand, there is virtually nothing to fear about hypervitaminosis and the limit is more of an economic type. Some of them deserve more attention in sportsmen and women:

- B1, especially in speed races, since this vitamin facilitates the entry of tricarboxylic elements in the Krebs cycle; on this, Topliff et al (1981) find that a high load of thiamine would tend to reduce hyperlactacidaemia;
- B2 which activates catabolism of lactic acid, (such as zinc) and which contributes to cellular oxidation of carbohydrates and lipids, in combination with niacin and pantothenic acid;
- B6, Bc (folic acid) and B12, because of their anti-anaemic role, but knowing that overdoses have no doping effect;
- Choline, which contributes, with vitamin B1, to the transmission of nerve impulses and is involved in the metabolism of fats (such as carnitine);

- H (biotin) which improves the quality of the horn of the hooves, in doses of 10 to 30 mg/d for 6 to 9 months (Comben et al, 1984 in Snow and Harris, 1989).

On the other hand, horses have no specific vitamin C requirements whereas it promotes the synthesis of carnitine and is tolerated in high doses and without disadvantages in the short-term.

In total, the usual mineral and vitamin requirements are quite well-known (Wolter, 1983). The work of muscles can increase them considerably, especially for the sodium lost in sweat, calcium with a view to improving bone solidity, selenium and vitamin E for preserving muscle integrity, magnesium and thiamine involved in energy metabolism, etc. Already, the increase in the level in food often offsets the gradually increasing requirements; however, safety margins can still be necessary to take account of the unequal effectiveness of the intakes, of individual variations in assimilation, additional requirements linked to different stresses. Beyond that, it appears completely illusory to practice overloads of minerals and/or of vitamins, as our tests on ponies have proven (Wolter et al, 1987), as well as the controls carried out in sportsmen and women (Weight et al, 1988a and b). These deliberate excesses vainly seek some ergogenic effect.

Ergogenic factors

These are non-essential nutritional factors which normally influence energy metabolism. In the hope of activating this and thereby of improving sporting performance, exogenic supplements are often wrongly recommended in the belief that endogenic production might limit maximum muscle performance in events at the highest level. However, it is not sufficient for one component to be visible in a metabolic process for its addition to food to be useful; a good example of this is ATP, the oral dosage of which (without knowing what happens to it during digestion) or indeed parenteral (in very low doses compared with the synthesis in the body) does not seem to be of any value, other than strictly commercial. In relation to this, any nutritional additive should have undergone specialised, objective and rigorous experimental controls, before being offered to a public which is too often uninformed, credulous and keen to make the most of any additional opportunity. The public is also quite easy to mislead with regard to the generally random, non-reproducible and unquantifiable results in real conditions. Furthermore, it is necessary to immediately eliminate any xenobiotic substance or any nutrient used in massive doses for the sole purpose of obtaining a pharmacodynamic effect similar to dosing.

Thiamine

For the purpose of increasing the nerve impulses and reducing the intramuscular accumulation of lactic acid during maximum anaerobic effort, this vitamin has been able to be used in quantities reaching 100 to 200 times the nutritional requirements.

Biotin

Biotin also intervenes in the entry of the products of glycolysis into the Krebs cycle; it does not seem capable of increasing the speed-threshold in practice (VLa4)[1], according to Lindner et al, 1992.

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[1] This is the speed corresponding to the lactic anaerobic threshold of 4 mmol-1

Cyanocobalamin
(B12), folic acids (Bc) and injectable iron (specifically in the form of iron dextran) are widely used in the hope of increasing the level of haemoglobin, or of myoglobin, and therefore the aerobic abilities. Their practical effectiveness remains very much under discussion and very transitory, to say the least. On the contrary, excess iron leads to an increased risk in metabolic peroxidation, including an accelerated use of vitamin E, predisposition to muscle lesions, lowering of immunity and sensitivity to stress.

Ascorbic acid
Vitamin C has sometimes been used in very high doses (up to 20 g per horse and per day according to Snow et al, 1987) to fight against the stress of long and renewed sporting events; but such use risks secondary negative effects, for example through exhaustion of the adrenals.

Selenium
Injectable, sometimes also used in heavy or over-repeated doses (on the pretext of improving the prevention of myositis and rhabdomyolysis) which could also lead to iatrogenic intoxication.

Aspartic and glutamic acids
These have the theoretical merit of stimulating the production of ATP (through the Krebs cycle of cellular oxidation). They would also enable hyperammoniaemia to be fought against (by promoting uropoiesis). In this case the addition of arginine would also be useful. However in comparison with endogenic production and the usual food consumption, a specialised supplement risks not having any appreciable influence in the long term on the level of these metabolites in the blood.

Ramified amino acids (valine, leucine and isoleucine) would be especially catabolised during the work of the muscle and, in return, might contribute to reducing the catabolism of proteins during effort. On the other hand, tryptophan, a serotonin precursor, should be considered more as a tranquillising factor than as a neuromuscular stimulant.

Carnitine
This carrier of long fatty acids through the mitochondrial membrane enables its metabolic oxidation; it is therefore necessary for aerobic muscular work and the prevention of hyperlipaemia, if not hypoglycaemia, hepatic insufficiency and cardiac problems. Its synthesis by the body seems easily achieved by lysine and methionine, in the presence of iron and vitamins PP, B6 and C; low in newborns, it increases with age and especially with training, as has been shown in thoroughbred horses (Foster et al, 1989). Renal deficiency does not seem very likely and does not seem to be in question beyond a predisposition to rhabdomyolysis (Van Den Haven et al, 1989). Moreover, supplementation in human patients deprived of exogenic intakes does not affect the oxidation of fatty acids (Bowyer et al, 1989)

except in babies under the age of 4 months (Olson et al, 1989). However, supplementation in form L rather than DL would be capable of raising the maximum VO_2 in humans (Angelini, in Hintz, 1989) but no improvement in endurance aptitude would result from this (Oyono-Enguelle et al, 1988). In horses, exercise does not change the muscle content of total carnitine (Foster and Harris, 1987). But the blood level of carnitine is increased to the maximum by a supplement of 15g of carnitine in food per horse and per day (Foster and Harris, 1989). Tests in our laboratory carried out on animals highly trained in endurance effort and well suited to hyperfatty diets have shown that supplementation of food with carnitine delays fatigue in ponies, both with the DL and L forms (not published).

Dimethylglycine (DMG)
Active ingredient of pangamic acid or vitamin B15 (where it is found combined with gluconic acid), the praises of DMG have been sung since 1964 firstly in the USSR then in the United States for particularly appealing properties concerning sportsmen and women; activation of metabolic oxidation and reduction of the accumulation of lactic acid with an increase of the anaerobic threshold, improvement of sporting performances and the speed of recovery, anti-stress effect and stimulation of immunity ... (Levine et al, 1982); Gannon and Kendall, 1982). In fact, the experimental results rarely reach those in the promotional documents: in humans in intense activity on a treadmill, Gray and Titlow (1982) report no benefit with DMG supplementation; in horses, Moffitt et al (1985) observe an interesting reduction in lactactemia. But both at Newmarket (Snow, personal communication) and in our laboratory, it was not possible to indicate any increase in the aptitude for sport.

I[n]osine
As a precursor of AMP, ADP-ATP, i[*n*]osine could theoretically be beneficial for energy metabolism and the work of muscles. However, our controls carried out in the laboratory in dogs and ponies show that inosine injections have no positive effect on sporting performance and only enable the acceleration of the speed of cardiac recovery, provided that intervention takes place in the minutes immediately preceding (not published).

Fish hydrolysates
Source of polypeptides and series ω3 fatty acids probably in a combined form which would be more absorbable, they are likely to strengthen significantly the aptitude for sport according to our experiments carried out in dogs and ponies, with an autolysate prepared in a very careful way being clearly superior compared with a commercial hydrolysate (not published).

Sodium bicarbonate
Shortly before anaerobic effort which may be in the form of a beverage (milk shake), to increase the buffer capacity against accumulation of lactic acid in the muscles, with a view to increasing stamina during effort (Lawrence et al, 1990; Carlson, 1990; Harkins and Kamerling, 1992). Parallel to the prevention of metabolic acidosis, this type of supplementation raises the urinary pH and reduces loss of calcium in urine (Baker et al, 1992; Stutz et al, 1992; Wall et al, 1992). To date, that practice is considered fraudulent and is prohibited in different countries.

Dimethylsulphoxide (DMSO)
DMSO and its metabolic precursor methylsulphonylmethane (MSM), which would be of interest in more prolonged activity, have anti-inflammatory properties used to best effect to fight against joint pains. They are not nutritional and come under the legislation on medicines.

Various phytotherapeutic preparations, based on Ginseng, eleutherococcus, harpagophytum, gingko, etc, with potential effectiveness but that would need to be tested by experiment. In the case of a pharmodynamic action, the question would be raised of their regulatory authorisation for use either in dietetics or in medicinal foodstuffs.

However, the anti-doping regulations have to accept the concept of threshold levels because it is not permitted to prohibit common raw materials such as:

- oats, which contain a tonic factor known for more than a century as 'avenine' but still of an unknown type;
- germinated barley which contains hordenine which also has stimulant properties parenterally, but is easily reabsorbed *per os*;
- alfalfa contains puric and pyrimidic bases, traces of arsenic and phyto-oestrogens.

On the other hand, it would require better control over the fraudulent use of anabolising hormones (including during rearing and training and not just in the race winners). Above all, to date it has become vital to control doping using β-agonists (Wolter, 1992), and erythropoietin.

In conclusion, an in-depth understanding of the nutritional requirements of the race horse have enabled specialised foodstuffs to be designed which are better suited to sporting activity and even to the type of effort made. Consequently, we can hope for a greater use of genetic opportunities, greater ability to develop more rigorous training and consequently clear progress in the level and the reproducibility of performance in horses.

References
[see original text for these]